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*Office Location: REM 5B19	erent Company Company Company
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\*Case serial number: 09/ 582,442 If not related to a patent application, please enter NA here.

256, 269, 274, 275 Class / Subclass(es) | 514 544/238, 295, 296, 298, 311, 317, 319, 320, 326, 329. Earliest Priority Filing Date: 12-26-97

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Query 9/582,442

$$G_{2} = G_{3}$$

$$G_{4}$$

$$G_{4}$$

$$G_{4}$$

$$G_{4}$$

$$G_{4}$$

$$G_{4}$$

$$G_{5}$$

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$$G_{5}$$

$$G_{7}$$

$$G_{8}$$

$$G_{8$$

-G,,G2,G3+G4 are independently NorCHbut at least one is N;

- X is CH or N;

- Y is N;

- Zy is -SOz- or - CHz-;

- Zz is a bond, alkylene, alkenylene or

-Q is a ring

See also attached Claims

PATENT 1110-0271P

N THE U.S. PATENT AND TRADEMARK OFFICE RECEIVED

Applicant:

NISHIDA, Hidemitsu et al.

Conf.:3582

JUN 1 3 2002

Appl. No.:

09/582,442

Group:

TECHCENTER 1600/2900

Filed:

June 26, 2000

Examiner: T. TRUONG

For:

AROMATIC COMPOUNDS HAVING CYCLIC AMINO GROUPS AND

SALTS THEREOF

# AMENDMENT UNDER 37 CFR 1.111

**Assistant Commissioner for Patents** Washington, DC 20231

June 12, 2002

Sir:

In reply to the Office Action of March 12, 2002, the following amendments and remarks are respectfully submitted in connection with the above-identified application.

# IN THE CLAIMS:

Please amend claims 1, 2, 6, and 17 to read:

1. (thrice amended) A method for treating a disease for which the FXa inhibitor is indicated, comprising: administering an effective amount of a composition comprising a pharmaceutical carrier and at least one compound represented by the following formula (I') or a salt thereof:

$$R_{2}$$
 $R_{3}$ 
 $R_{6}$ 
 $R_{7}$ 
 $R_{1}$ 
 $R_{2}$ 
 $R_{3}$ 
 $R_{6}$ 
 $R_{7}$ 
 $R_{7}$ 
 $R_{1}$ 
 $R_{2}$ 
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 $R_{7}$ 
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 $R_{7}$ 
 $R_{7}$ 
 $R_{8}$ 
 $R_{9}$ 
 $R_{9}$ 
 $R_{9}$ 

wherein  $G_1$ ,  $G_2$ , and  $G_3$  are independently CH or N and  $G_4$  is CH, provided that one or two of  $G_1$  to  $G_3$  is N;

X is CH and Y is N;

Z<sub>1</sub> is a group represented by the formula -SO<sub>2</sub>- or -CH<sub>2</sub>-;

 $Z_2$  is a single bond, a lower alkylene group, a lower alkenylene group or a lower alkynylene group;

Q is an optionally substituted aryl group in the form of a monocyclic or fused hydrocarbon ring having 6-14 carbon atoms or an optionally substituted heteroaryl group in a monocyclic or fused cyclic form having 1-4 heteroatoms selected from the group consisting of oxygen, sulfur, and nitrogen atoms;

R<sub>1</sub> is either any substituent selected from group A (a hydrogen atom; a halogen atom; a trifluoromethyl group; a trifluoromethoxy group; a carboxyl group; a carbamoyl group; an amino group; a cyano group; a nitro group; a lower alkanoyl group; a lower alkoxy group; a lower alkoxycarbonyl group; a mono- or di-substituted lower alkylamino group; a cyclic amino group optionally substituted by a lower alkyl group or a hydroxyl group and being a pyrrolidinyl group, a piperidinyl group, a morpholino group, or a piperazinyl group; a lower alkanoylamino group; a phenyl group; a phenoxy group; a benzyloxy group; a benzoyl group; a mercapto group; a lower alkylthio group; a lower alkylthiocarbonyl group; a hydroxyl group; or a mono- or di-substituted lower alkylaminocarbonyl group), or an oxygen atom that forms a N-oxide group with N in any one of G1 – G4, or a lower alkyl group or a lower alkenyl group that may be substituted with a desired number of substituents of group A or a lower alkoxy group or a lower alkoxy group A or a lower alkoxy group;

each of R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub> and R<sub>9</sub> forms an oxo group when combined with the carbon atom on the ring to which they are bound, or they are each a hydrogen atom, a carboxyl group, a lower alkylcarbonyl group, a lower

DI

alkoxycarbonyl group, a lower alkoxycarbonylalkylcarbonyl group, an optionally mono- or di-lower alkyl substituted carbamoyl group, a lower alkoxycarbamoyl group, a lower alkoxycarbonylalkylcarbamoyl group, a pyrrolidin-1-ylcarbonyl group, a morpholinocarbonyl group, a piperazin-1-ylcarbonyl group that may be substituted by a methyl group in 4-position, a piperidin-1-ylcarbonyl group that may be substituted by a methyl group or a hydroxyl group in 4-position, an N-phenylcarbamoyl group or a group represented by the formula -  $CONH(CH_2)_pS(O)_qR_{10}$  or  $-CONH(CH_2)_rNR_{11}R_{12}$ , or a lower alkyl group that may be substituted by  $R_{15}$ ;

each of  $R_{10}$ ,  $R_{11}$  and  $R_{12}$  independently represents a hydrogen atom, a lower alkyl group, a phenyl group or a lower alkylphenyl group;

R<sub>15</sub> is a carboxyl group, a lower alkoxycarbonyl group, a hydroxyl group, a lower alkoxy group, a lower alkanoyloxy group, an amino group, a mono- or disubstituted lower alkylamino group, a lower alkanoylamino group, a lower alkylsulfonylamino group, a cyclic amino group optionally substituted by a lower alkyl group or a hydroxyl group and being a pyrrolidinyl group, a piperidinyl group, a morpholino group, or a piperazinyl group, or an N-hydroxyimino group;

provided that R<sub>6</sub> may also represent two lower alkyl groups in geminal;

also provided that if any one of the substituents R<sub>2</sub> - R<sub>9</sub> includes cyclic group, such cyclic group may be substituted by one or two lower alkyl groups;

m is an integer of 0 - 3 and n is 1, p is an integer of 0 - 4, q is an integer of 0 - 2, and r is an integer of 1 - 4.

2. (thrice amended) The method according to claim 1, wherein the substituent of the optionally substituted aryl or heteroaryl group as Q of the formula (I') is 1 - 4 groups in any combinations that are selected from among substituents of either group B (a halogen atom, a trifluoromethyl group, a trifluoromethoxy group, a trifluoromethanesulfonyl group, a carboxyl group, a carboxyl group, a carboxyl group, a lower alkoxyl group, a lower alkoxycarbonyl group, a mono- or digroup, a lower alkoxyl group, a lower alkoxycarbonyl group, a mono- or digroup, a lower alkoxyl group, a lower alkoxycarbonyl group, a mono- or digroup, a lower alkoxyl group, a lower alkoxycarbonyl group, a mono- or digroup.



# 21 | |PS |

BOX AF PATENT 1110-0271P

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant: NISHIDA, Hidemitsu et al.

Conf.:

3582

Appl. No.: 09/582,442

Group:

1624

Filed:

June 26, 2000

Examiner: T. TRUONG

For:

AROMATIC COMPOUNDS HAVING CYCLIC AMINO GROUPS AND

SALTS THEREOF

# AMENDMENT PURSUANT TO 37 CFR 1.607

Box AF

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

June 11, 2003

Sir:

The following amendments and remarks are respectfully submitted in connection with the above-identified application.

## IN THE CLAIMS:

Please add the following new claims:

Fi

(New) A compound represented by the following

formula (I) or a salt thereof:

06/12/2003 ZJUHAR1 00000023 09582442

01 FC:1201 02 FC:1202 168.00 OP 270.00 OP

Application No.: 09/582,442

$$R_{2}$$
 $R_{2}$ 
 $R_{3}$ 
 $R_{6}$ 
 $R_{7}$ 
 $R_{1}$ 
 $R_{2}$ 
 $R_{3}$ 
 $R_{6}$ 
 $R_{7}$ 
 $R_{1}$ 
 $R_{2}$ 
 $R_{3}$ 
 $R_{6}$ 
 $R_{7}$ 
 $R_{1}$ 
 $R_{2}$ 
 $R_{2}$ 
 $R_{3}$ 
 $R_{4}$ 
 $R_{5}$ 
 $R_{8}$ 
 $R_{9}$ 
 $R_{9}$ 
 $R_{1}$ 

## wherein

at least one of  $G_1$ ,  $G_2$ ,  $G_3$  and  $G_4$  is N and the remaining are independently CH or N;

X is CH or N;

Y is N;

 $Z_1$  is a group represented by the formula -SO<sub>2</sub>-;

Z<sub>2</sub> is a single bond;

Q is an aryl group being unsubstituted or substituted with 1 to 4 substituents selected from the group consisting of the Group B or a lower alkyl group that may be substituted by a desired number of substituents of Group B, wherein Group B is:

- a halogen atom,
- a trifluoromethyl group,
- a trifluoromethanesulfonyl group,
- a carbamoyl group,
- an amino group,
- a cyano group,
- a nitro group,
- a lower alkanoyl group,

- a lower alkoxyl group,
- a lower alkoxycarbonyl group,
- a mono- or di-substituted lower alkylamino group,
- a lower alkanoylamino group,
- a cyclic amino group,
- a mercapto group,
- a lower alkylthio group,
- a lower alkylsulfonyl group,
- a hydroxyl group or a mono- or di-substituted lower alkylaminocarbonyl group,
  - an amidino group,
  - a group of the formula -NHCR<sub>13</sub>-NHR<sub>14</sub>

wherein R<sub>13</sub> is an optionally

cyano-substituted imino group or a group =CHNO<sub>2</sub>;

 $R_{14}$  is a hydrogen atom or a methyl group,

- a phenyl group,
- a heteroaryl group,
- a heteroaryloxy group, or
- or a group represented by heteroaryl-S(0)t,

wherein t is an integer of 0 - 2,

aromatic monocyclic group containing not more than four oxygen atoms, sulfur atoms or nitrogen atoms, provided that

all aromatic rings of Group B may be mono-, di-, or trisubstituted by any substituent of Group C,
wherein Group C is
a halogen atom,
a hydroxyl group,
an amino group,

a mono- or di-substituted lower alkylamino group,

a cyclic amino group,

a mono- or di-substituted lower alkylaminocarbonyl group,

a lower alkyl group,

a lower alkoxy group or

 $R_1$  is any substituent selected from group A wherein Group A is

- a hydrogen atom,
- a halogen atom,
- a trifluoromethyl group,
- a carbamoyl group,
- an amino group,
- a cyano group,
- a nitro group,
- a lower alkanoyl group,
- a lower alkoxy group,
- a lower alkoxycarbonyl group,

- a mono- or di-substituted lower alkylamino group,
- a cyclic amino group,
- a lower alkanoylamino group,
- a phenyl group,
- a benzoyl group,
- a mercapto group,
- a lower alkylthio group,
- a hydroxyl group or
- a mono- or di-substituted lower alkylamino- carbonyl group,  $R_1$  may also be an oxygen atom that forms a N-oxide group with N in any one of  $G_1$   $G_4$ , or a lower alkyl group, a lower alkoxy group or a lower alkenyl group that may be substituted with a desired number of substituents selected from
  - a hydrogen atom,
  - a halogen atom,
  - an amino group,
  - a cyano group,
  - a lower alkoxy group,
  - a mono- or di-substituted lower alkylamino group,
  - a lower alkanoylamino group, or
  - a hydroxyl group;

one of  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$  is hydrogen and the remaining are selected from a lower alkoxycarbonyl group, an optionally

mono- or di-lower alkyl substituted carbamoyl group, an N-phenylcarbamoyl group or a group represented by the formula  $-\text{CONH}(\text{CH}_2)_P S(O)_q R_{10}$  or  $-\text{CONH}(\text{CH}_2)_r N R_{11} R_{12}$ , or a lower alkyl group that may be substituted by  $R_{15}$ ;

R<sub>6</sub> forms a carbonyl group with the carbon atom on the ring to which it is attached;

each of  $R_7$ ,  $R_8$  and  $R_9$  is a hydrogen atom, a lower alkoxycarbonyl group, an optionally mono- or di-lower alkyl substituted carbamoyl group, an N-phenylcarbamoyl group or a group represented by the formula  $-\text{CONH}(\text{CH}_2)_P S(0)_q R_{10}$  or  $-\text{CONH}(\text{CH}_2)_r N R_{11} R_{12}$ , or a lower alkyl group that may be substituted by  $R_{15}$ ;

each of  $R_{10}$ ,  $R_{11}$  and  $R_{12}$  independently represents a hydrogen atom, a lower alkyl group, a phenyl group or a lower alkylphenyl group;

 $R_{15}$  is a carboxyl group, a hydroxyl group, or an amino group;

m and n are independently an integer of 0-3,

p is an integer of 0-4,

q is an integer of 0-2, and

r is an integer of 1-4;

provided that if any one of the substituents  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ ,  $R_7$ ,  $R_8$ , or  $R_9$  includes a cyclic group, such cyclic group may be substituted by one or two lower alkyl groups.

FI